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ORIGINAL RESEARCH

Joint Effect of Central Obesity and Family History on Hypertension in Type 2 Diabetes: A Cross-Sectional Study in China

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Purpose: This study aimed to examine the joint effect of central obesity (CO) and family history of hypertension (FHH) on hypertension in Chinese patients with type 2 diabetes mellitus (T2DM).

Methods: A total of 1756 T2DM patients were enrolled from a cross-sectional study conducted in Zhejiang Province, China (March - November 2018). Multivariate logistic regression models were used to analyze factors associated with hypertension and to assess CO-FHH interactions on both additive and multiplicative scales. Associations between waist circumference (WC) and systolic/diastolic blood pressure (SBP/DBP) were evaluated using generalized additive models (GAM) and Spearman correlation. The relationship between WC and hypertension was further explored using restricted cubic splines (RCS).

Results: The prevalence of hypertension was 64.52%. WC was positively correlated with SBP (r = 0.25, P<0.001) and DBP (r=0.27, P<0.001), and showed a linear association with hypertension in both sexes (P for non-linearity>0.05). After adjusting for potential covariates, T2DM patients with both CO and FHH had a 4.64-fold higher risk of hypertension (95% CI: 3.22–6.67) compared to the reference group. A statistically significant additive interaction between CO and FHH was observed, with a relative excess risk due to interaction (RERI) of 1.59 (95% CI: 0.39–3.19), an attributable proportion (AP) of 0.34 (95% CI: 0.08–0.51), and a synergy index (SI) of 1.78 (95% CI: 1.13–2.79). No statistically significant multiplicative interaction was found.

Conclusion: CO and FHH may jointly contribute to hypertension in Chinese T2DM patients through an additive effect beyond their individual associations. Maintaining a healthy WC is especially important for T2DM patients with a family history of hypertension.

Keywords: central obesity, hypertension, interaction, family history of hypertension, type 2 diabetes mellitus, waist circumference

Introduction

The global prevalence of type 2 diabetes mellitus (T2DM) has risen to epidemic levels, with the number of affected individuals continuously increasing over the past decades. In mainland China, the prevalence of T2DM in 2017 was reported as 12.8% based on the American Diabetes Association criteria and 11.2% according to the World Health Organization standards.[1] This chronic disease presents significant public health challenges by contributing to increased morbidity and mortality and imposing a substantial economic burden on healthcare systems worldwide.[2] Hypertension frequently coexists with T2DM, with studies reporting a prevalence of 59.9% among T2DM patients in China,[3] and approximately 50% in Japan.[4] Hypertension not only exacerbates the microvascular and macrovascular complications of T2DM but also significantly increases the risk of cardiovascular disease in these patients. These findings underscore the importance of identifying modifiable risk factors to reduce the public health burden associated with T2DM and hypertension.[5]

Central obesity (CO), characterized by excessive fat accumulation around the abdominal region, is widely acknowledged as a key risk factor for hypertension. Previous research has consistently demonstrated that CO is associated with increased blood pressure (BP) through mechanisms such as heightened insulin resistance (IR), activation of the renin-

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angiotensin-aldosterone system (RAAS), and increased sympathetic nervous system (SNS) activity.[6] Family history of hypertension (FHH) is another crucial factor influencing the risk of hypertension and other cardiovascular conditions. FHH reflects the interplay between genetic susceptibility and shared environmental exposures, serving as an important risk factor for obesity, diabetes and various cardiovascular diseases.

Although strong evidence supports the individual associations of CO and FHH with hypertension, their combined effect, particularly among patients with T2DM, remains inadequately explored. Few studies have quantified their interaction or assessed whether CO modifies the FHH-related risk of hypertension. Addressing this knowledge gap is essential, as understanding their joint impact could inform more targeted preventive strategies and clinical interventions for high-risk individuals. Therefore, this study aims to investigate the interactive effect of CO and FHH on hypertension among Chinese patients with T2DM.

Material and Methods

Study Design and Population

This research was conducted from March to November 2018 in Zhejiang Province, eastern China, as part of the China National Diabetic Complications Study. Detailed information on the study design, methodology, and participant characteristics has been reported previously.[7] Briefly, the study included individuals aged ≥18 years with T2DM who had lived in the selected areas for at least six months in the previous year.

A multi-stage random sampling method was employed. First, two districts and two counties were randomly selected from Zhejiang Province. Within each selected district or county, four streets or towns were randomly chosen. Then, from each selected street or town, 120 T2DM patients registered in the local healthcare system were randomly sampled. The selection was stratified by sex and age, yielding a total of 1,920 participants. Each participant underwent a comprehensive physical examination, fasting blood sample collection, and a structured face-to-face questionnaire interview. The detailed participant selection process is illustrated in Figure 1.

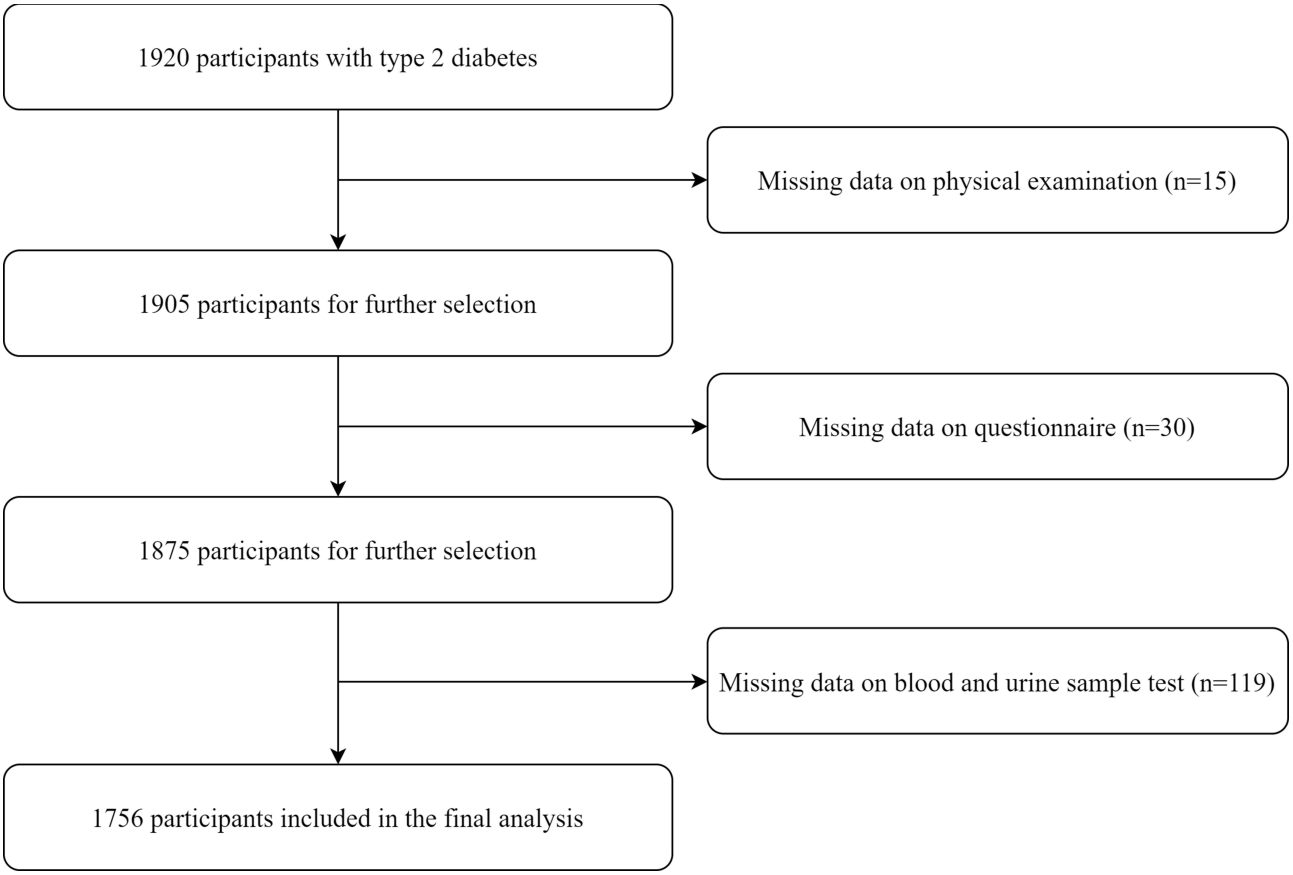

Figure 1 The selection procedure of participants.

Data Collection

Standardized data collection was conducted by trained personnel from local health centers through face-to-face interviews to gather information on demographic characteristics, lifestyle factors, and family history. This was followed by physical examinations conducted by certified healthcare providers using calibrated instruments. Anthropometric measurements included height (measured to 0.1 cm using a TZG brand stadiometer), weight (recorded to 0.1 kg using an HD-390 electronic scale; TANITA, Japan), and waist circumference (WC; measured to 0.1 cm at the midpoint between the lower rib and iliac crest during normal expiration). Blood pressure was measured after 5 minutes of seated rest using an automated OMRON HBP-1300 sphygmomanometer (OMRON, Japan). Three readings were taken at 1-minute intervals, and the average of the three was used for analysis. Fasting venous blood samples were collected for biochemical analyses, including fasting plasma glucose (FPG; hexokinase method), hemoglobin A1c (HbA1c; high-performance liquid chromatography using a Bio-Rad D10 analyzer; Bio-Rad, USA), and lipid profile, including total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C), measured enzymatically using a Roche cobas c701 analyzer (Roche, Switzerland).

Definition of Variables

Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg, diastolic blood pressure (DBP) ≥90 mmHg, or a self-reported history of hypertension. Family history of hypertension was defined as having at least one parent or sibling with the condition. Central obesity was defined as a WC ≥90 cm for men or ≥85 cm for women. Participants were grouped by age as follows: young adults (18–44 years), middle-aged adults (45–59 years), and elderly adults (≥60 years). Educational level was categorized as secondary school or below, senior high school, and college or above. Residence was classified as urban or rural. Current smoking was defined as daily or occasional cigarette use. Alcohol consumption was defined as drinking within the past 30 days. Unfavorable lipid profiles were diagnosed as: TC ≥6.22 mmol/L, TG ≥2.26 mmol/L, LDL-C ≥4.14 mmol/L, or HDL-C <1.04 mmol/L. Abnormal FPG and HbA1c levels were defined as ≥7.0 mmol/L and ≥7.0%, respectively.

Statistical Methods

Quantitative data were expressed as mean ± standard deviation for normally distributed variables or median (interquartile range) for non-normally distributed variables. Group comparisons were performed using the *t*-test or Wilcoxon rank-sum test, as appropriate. Categorical variables were presented as frequency (percentage), and group differences were assessed using the chi-square (χ^2) test. An unconditional multivariate logistic regression model was used to identify factors associated with hypertension. The backward elimination method was applied to retain significant variables in the final model. The association between WC and SBP/DBP was examined using the generalized additive model (GAM) and Spearman correlation analysis. The relationship between WC and hypertension was further evaluated using restricted cubic splines (RCS), stratified by sex, with reference values set at 90.0 cm for men and 85.0 cm for women. The interaction between CO and FHH was assessed on both multiplicative and additive scales.[8,9] For additive interaction, CO and FHH were included in the logistic regression model as both independent and interactive variables. Participants were categorized into four groups based on CO and FHH status: non-CO & non-FHH, non-CO & FHH, CO & non-FHH, and CO & FHH. Measures of additive interaction, including the relative excess risk due to interaction (RERI), attributable proportion (AP), and synergy index (SI), were calculated, with 95% confidence intervals (CIs) estimated using Anderson's method.[10] A RERI >0 indicates a positive additive interaction, whereas CIs for RERI or AP that include 0, or CIs for SI that include 1, suggest no additive interaction.[11] The CO × FHH interaction term was also included in logistic regression models to test multiplicative interaction, with significance assessed using odds ratios (ORs). Sensitivity analyses were conducted using the waist-to-height ratio (WHtR > 0.5) as an alternative definition of CO[12] to assess the robustness of the findings. A two-sided p-value <0.05 was considered statistically significant. All analyses were performed using SAS software (version 9.4; SAS Institute Inc., Cary, NC, USA).

Results

Basic Characteristics of the Subjects

A total of 1,756 participants with complete data were included in the study. The mean age was 57.23 ± 10.15 years, with an average body mass index (BMI) of 24.76 ± 3.43 kg/m2 and a mean WC of 87.33 ± 9.52 cm. Table 1 summarizes the general characteristics of the participants. Of the total participants, 876 (49.89%) participants were male. Hypertension was identified in 1,133 (64.52%) participants, CO in 873 (49.72%), and FHH in 1,132 (64.46%). Central obesity and FHH were more prevalent in the hypertensive group compared to the non-hypertensive group. Significant differences were also observed between the hypertension and non-hypertension groups in terms of age, educational level, WC, BMI, TG, HDL-C, HbA1c, and alcohol consumption ($p < 0.05$).

Table 1 Basic Characteristics of the Subjects Classified by Hypertension (n=1,756)

Variables	Overall (n,%)	Group without Hypertension (n,%)	Group with Hypertension (n,%)	$t/\chi^2/z$	*P* Value
Number of cases, n(%)	1,756 (100)	623 (35.48)	1,133 (64.52)		
Age, years, mean (SD)	57.23 (10.15)	52.87 (10.75)	59.62 (8.95)	−13.33[a]	<0.001
Sex, n(%)				2.48[b]	0.115
Male	876 (49.89)	295 (47.35)	581 (51.28)		
Female	880 (50.11)	328 (52.65)	552 (48.72)		
Age group, n(%)				158.68[b]	<0.001
18~44	263 (14.98)	164 (26.32)	99 (8.74)		
45~59	767 (43.68)	308 (49.44)	459 (40.51)		
≥60	726 (41.34)	151 (24.24)	575 (50.75)		
Educational level, n(%)				12.14[b]	0.002
Secondary school and lower	1,541 (87.76)	531 (85.23)	1010 (89.14)		
Senior high school	171 (9.74)	66 (10.59)	105 (9.27)		
College or above	44 (2.50)	26 (4.17)	18 (1.59)		
Resident place, n(%)				0.31[b]	0.579
Rural	875 (49.83)	316 (50.72)	559 (49.34)		
Urban	881 (50.17)	307 (49.28)	574 (50.66)		
Duration of diabetes(years), n(%)				2.96[b]	0.398
<=5	836 (47.61)	310 (49.76)	526 (46.42)		
6–10	491 (27.96)	162 (26.00)	329 (29.04)		
11–15	236 (13.44)	79 (12.68)	157 (13.86)		
>15	193 (10.99)	72 (11.56)	121 (10.68)		
WC, cm, mean (SD)	87.33 (9.52)	83.96 (9.18)	89.18 (9.19)	−11.41[a]	<0.001
Central obesity, n(%)	873 (49.72)	217 (34.83)	656 (57.90)	85.56[b]	<0.001
BMI, kg/m^2, mean (SD)	24.76 (3.43)	23.69 (3.22)	25.35 (3.41)	−10.00[a]	<0.001
SBP, mmHg, mean (SD)	136.45 (18.71)	121.44 (10.79)	144.71 (16.92)	−35.09[a]	<0.001
DBP, mmHg, mean (SD)	78.39 (10.68)	72.79 (8.01)	81.47 (10.72)	−19.21[a]	<0.001
Family history of hypertension, n(%)	1132 (64.46)	326 (52.33)	806 (71.14)	62.09[b]	<0.001
TG, mmol/L, median(IQR)	1.60 (1.12–2.42)	1.43 (1.00–2.12)	1.70 (1.21–2.62)	−6.59[c]	<0.001
TC, mmol/L, mean (SD)	4.65 (1.07)	4.61 (1.00)	4.69 (1.11)	−1.52[a]	0.130
HDL-C, mmol/L, mean (SD)	1.25 (0.36)	1.30 (0.37)	1.22 (0.35)	3.94[a]	<0.001
LDL-C, mmol/L, mean (SD)	2.73 (0.90)	2.75 (0.87)	2.72 (0.91)	0.67[a]	0.502
FPG, mmol/L, mean (SD)	7.94 (2.58)	8.05 (2.76)	7.88 (2.47)	1.28 [a]	0.202
HbA1c, %, mean (SD)	7.27 (1.49)	7.40 (1.67)	7.20 (1.37)	2.57[a]	0.010
Cigarette smoking, n(%)	436 (24.83)	170 (27.29)	266 (23.48)	3.126[b]	0.077
Alcohol drinking, n(%)	646 (36.79)	204 (32.74)	442 (39.01)	6.788[b]	0.009

Notes: [a]Student's *t*-test, [b]Chi-square test, [c]Wilcoxon rank-sum test.

Abbreviations: WC, waist circumference; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; TC, total cholesterol; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; FPG, fasting plasma glucose.

The Association Between CO and FHH on Hypertension

Table 2 demonstrates that in univariate logistic regression analysis, CO (OR = 2.57, 95% CI: 2.10–3.15) and a FHH (OR = 2.25, 95% CI: 1.83–2.75) were significantly associated with an elevated prevalence of hypertension. In multivariate logistic regression analysis adjusting for age and sex, this association remained statistically significant. Furthermore, after controlling for confounding factors such as age, sex, BMI, educational level, TG abnormal, HDL-C abnormal, HbA1c abnormal, alcohol drinking, and cigarette smoking, CO (OR = 1.92, 95% CI: 1.45–2.53) and a FHH (OR = 2.49, 95% CI: 1.99–3.12) continued to show a significant positive association with hypertension prevalence.

The Association Between WC and BP

A generalized additive model was employed to plot the fitted curve between SBP and WC, and between DBP and WC (Figure 2A and B). The figure demonstrates that both SBP and DBP increased with higher WC values. Consistently, Spearman's rank correlation indicated a positive relationship between WC and SBP (correlation coefficient = 0.25, $P < 0.001$) and between WC and DBP (correlation coefficient = 0.27, $P < 0.001$).

The Association Between WC and Hypertension

A RCS analysis was used to examine the relationship between WC and hypertension. The reference value (OR = 1.00) for WC was set at 90.0 cm for males and 85.0 cm for females. This analysis, adjusted for age, sex, BMI, educational level, TG abnormal, HDL-C abnormal, HbA1c abnormal, alcohol consumption, and cigarette smoking, showed a linear relationship between WC and hypertension in both males (p for non-linearity = 0.993) and females (p for non-linearity = 0.154) (Figure 3A and B).

The Interaction Analysis of CO and FHH on Hypertension

Table 3 demonstrates that in the crude model, participants with both CO and family history of hypertension (FHH) exhibited a 5.53-fold higher hypertension risk (95% CI: 4.11–7.44) compared to the reference group (non-CO & non-FHH). This risk estimate significantly exceeded those observed in either the non-CO & FHH group or the CO & non-FHH group. After adjustment for age and sex, the multivariable-adjusted odds ratio (OR) for the CO & FHH group increased to 6.72 (95% CI: 4.89–9.24). In the fully adjusted model controlling for age, sex, BMI, educational attainment, TG abnormal, HDL-C abnormal, HbA1c abnormal, alcohol consumption, and smoking status, the CO & FHH group maintained a substantially elevated risk (OR = 4.64; 95% CI: 3.22–6.67), which remained markedly higher than the adjusted risks in both the non-CO & FHH group (OR = 2.32; 95% CI: 1.72–3.13) and the CO & non-FHH group (OR = 1.73; 95% CI: 1.17–2.55).

Interaction analysis was performed to evaluate potential synergistic effects between CO and FHH on hypertension risk (Table 4). On the additive scale, all three interaction measures (RERI, AP, and SI) demonstrated statistically significant positive associations in both unadjusted and adjusted models. These measures remained remarkably stable across model specifications: in the crude model, after adjustment for age and sex, and in the fully adjusted model incorporating age, sex, BMI, education

Table 2 Independent Effects of Central Obesity and Family History of Hypertension on the Risk of Hypertension

Variables	Non-Hypertension Group (n,%)	Hypertension Group (n,%)	OR_1[a] (95% CI)	OR_2[b] (95% CI)	OR_3[c] (95% CI)
CO					
No	406 (65.17)	477 (42.10)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	217 (34.83)	656 (57.90)	2.57 (2.10–3.15)	2.77 (2.23–3.43)	1.92 (1.45–2.53)
FHH					
No	297 (47.67)	327 (28.86)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	326 (52.33)	806 (71.14)	2.25 (1.83–2.75)	2.52 (2.03–3.13)	2.49 (1.99–3.12)

Notes: [a]OR_1: univariate analysis; [b]OR_2: multivariate analysis, adjusted for age and sex; [c]OR_3: multivariate analysis, adjusted for age, sex, BMI, education level, TG abnormal, HDL-C abnormal, HbA1c abnormal, alcohol drinking, and cigarette smoking.
Abbreviations: CO, central obesity; FHH, family history of hypertension; OR, odds ratio; CI, confidence interval.

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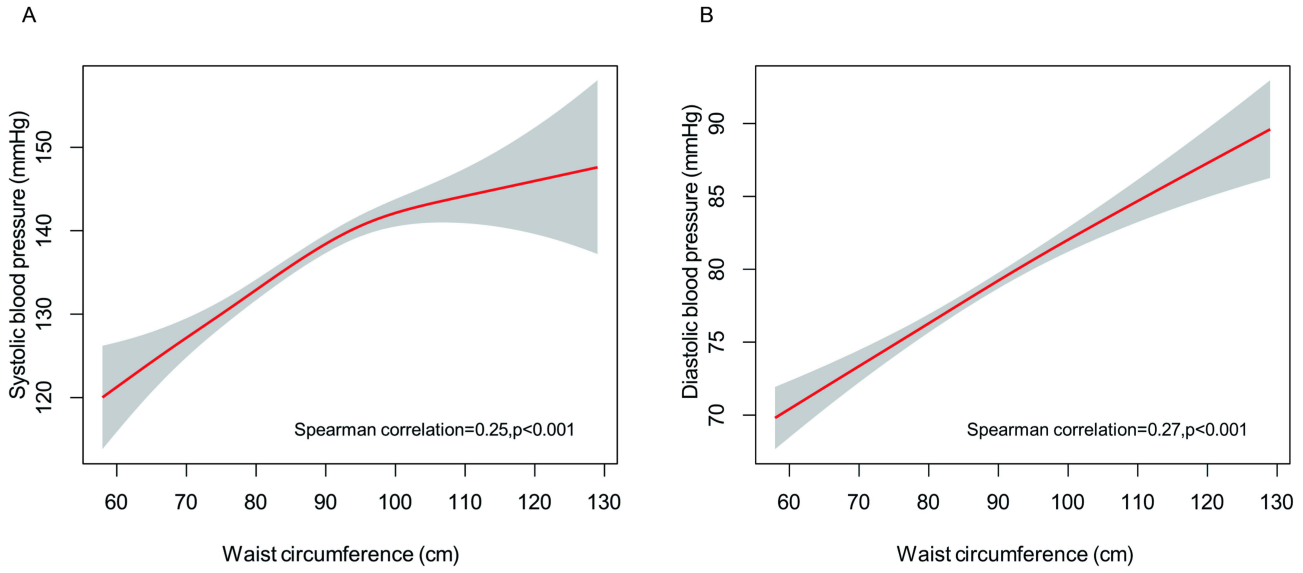

Figure 2 Association between waist circumference (WC) and both systolic blood pressure (SBP) and diastolic blood pressure (DBP), with 95% confidence intervals (CIs). (**A**) Association between WC and SBP. (**B**) Association between WC and DBP. The red solid lines represent the fitted curves illustrating the trends in these associations. The grey shaded areas represent the 95% CIs around the fitted curves, indicating the precision of the estimated relationships.

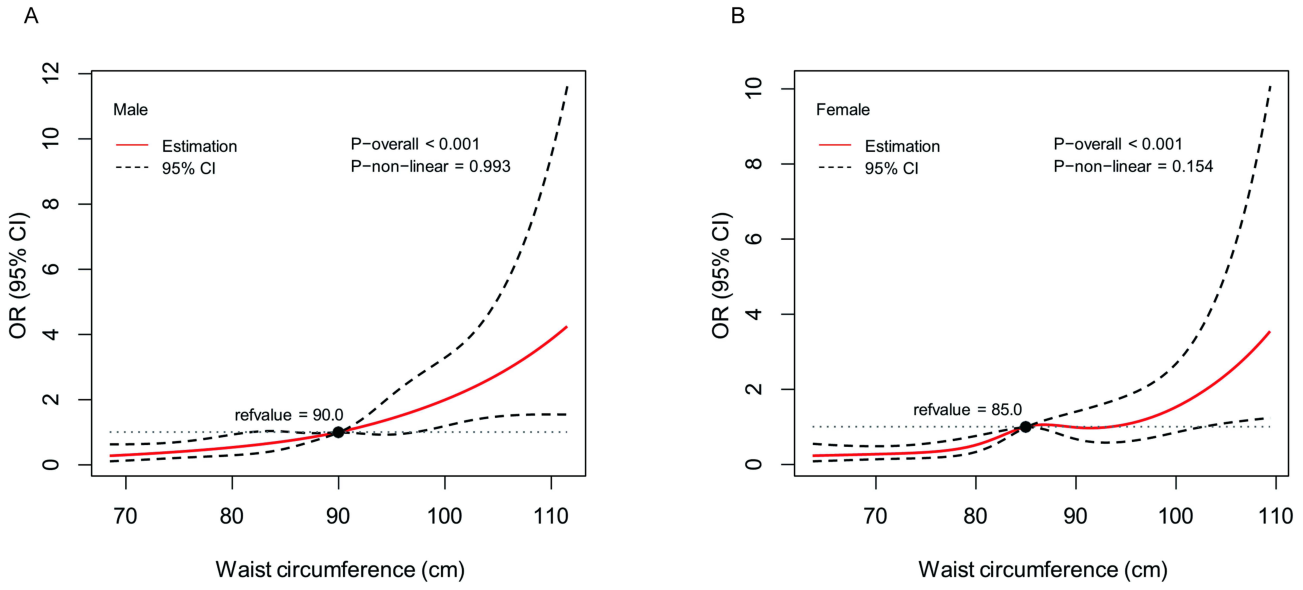

Figure 3 The association between waist circumference (WC) and hypertension in males and females, with 95% confidence intervals (CIs). The model shows odds ratios (ORs) compared with WC = 90.0 cm in males and WC = 85.0 cm in females, adjusting for age, sex, body mass index (BMI), education level, abnormal triglycerides, abnormal high-density lipoprotein cholesterol, abnormal hemoglobin A1c, alcohol drinking, and cigarette smoking. The red solid lines represent the fitted curves between WC and hypertension. The dotted horizontal lines indicate an odds ratio of 1. The dashed lines represent the 95% confidence intervals for the fitted curve. (**A**) The association between WC and hypertension in males. (**B**) The association between WC and hypertension in females.
Abbreviation: OR, odds ratio.

level, TG abnormal, HDL-C abnormal, HbA1c abnormal, alcohol consumption, and smoking status. The fully adjusted model yielded the following estimates: RERI = 1.59 (95% CI: 0.39–3.19), AP = 0.34 (95% CI: 0.08–0.51), and SI = 1.78 (95% CI: 1.13–2.79). These results indicate that 1.59-fold of the total 4.64-fold increased hypertension risk in the CO & FHH group was specifically attributable to their interaction effect, corresponding to 34% (AP) of the total risk being explained by this interaction. In contrast, multiplicative scale analysis revealed no statistically significant interaction effects in any model specification.

Table 3 Multivariate Logistic Regression Models of the Joint Effect of Central Obesity and Family History of Hypertension on Hypertension

Models	Variables		OR (95% CI)	ORs (95% CI) of FHH within the Strata of CO	ORs (95% CI) of CO within the Strata of FHH
	CO	FHH			
Crude	No	No	1.00(ref)		
		Yes	2.03 (1.54–2.68)	2.03 (1.54–2.68)	
	Yes	No	2.27 (1.65–3.14)		2.27 (1.65–3.14)
		Yes	5.53 (4.11–7.44)	2.43 (1.77–3.34)	2.72 (2.08–3.55)
Model 1	No	No	1.00(ref)		
		Yes	2.33 (1.73–3.12)	2.33 (1.73–3.12)	
	Yes	No	2.54 (1.79–3.58)		2.54 (1.79–3.58)
		Yes	6.72 (4.89–9.24)	2.65 (1.89–3.71)	2.89 (2.18–3.82)
Model 2	No	No	1.00(ref)		
		Yes	2.32 (1.72–3.13)	2.32 (1.72–3.13)	
	Yes	No	1.73 (1.17–2.55)		1.73 (1.17–2.55)
		Yes	4.64 (3.22–6.67)	2.68 (1.91–3.77)	2.00 (1.43–2.80)

Notes: Crude: unadjusted for any covariate; Model 1: adjusted for age, sex; Model 2: adjusted for age, sex, BMI, education level, TG abnormal, HDL-C abnormal, HbA1c abnormal, alcohol drinking, and cigarette smoking.
Abbreviations: CO, central obesity; FHH, family history of hypertension; OR, odds ratio; CI, confidence interval.

Table 4 Interaction Effect Indicators of Central Obesity and Family History of Hypertension on Hypertension

Models	Effect Value			
	Additive Scale			Multiplicative Scale
	RERI (95% CI)	AP (95% CI)	SI (95% CI)	OR (95% CI)
Crude	2.22 (0.98–3.77)	0.40 (0.19–0.55)	1.96 (1.31–2.94)	1.20 (0.79–1.82)
Model 1	2.86 (1.31–4.89)	0.43 (0.22–0.57)	2.00 (1.35–2.95)	1.14 (0.73–1.77)
Model 2	1.59 (0.39–3.19)	0.34 (0.08–0.51)	1.78 (1.13–2.79)	1.16 (0.74–1.82)

Notes: Crude: unadjusted for any covariate; Model 1: adjusted for age, sex; Model 2: adjusted for age, sex, BMI, education level, TG abnormal, HDL-C abnormal, HbA1c abnormal, alcohol drinking and cigarette smoking.
Abbreviations: OR, odds ratio; CI, confidence interval; RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction; SI, synergy index.

Sensitivity Analysis

Sensitivity analysis, using WHtR > 0.5 as an alternative measure for CO, is presented in Table 5. In the final model, the values for RERI, AP, and SI were 2.09 (95% CI: 1.00–3.87), 0.44 (95% CI: 0.23–0.61), and 2.29 (95% CI: 1.30–4.04), respectively. Similar to the primary analysis, no significant interaction effects were detected on the multiplicative scale. These results are consistent with the primary findings, reinforcing the robustness and validity of the study's conclusions.

Discussion

The global rise in T2DM prevalence is accompanied by an increasing prevalence of hypertension among patients with T2DM, a critical comorbidity that worsens cardiovascular risk.[13] In our study, we observed a notably high prevalence of hypertension in patients with T2DM (64.52%), which is significantly higher than the 24.7% prevalence observed in the general Chinese population in 2018,[14] and consistent with findings from other studies on hypertension prevalence in T2DM populations.[4,15,16] This disparity highlights the elevated risk of hypertension associated with diabetic pathophysiology, including IR, chronic hyperglycemia, and related metabolic disturbances.[17]

Table 5 Sensitivity Analysis of the Interaction Effects Between Central Obesity and Family History of Hypertension on Hypertension

Models	Effect Value			
	Additive Scale			Multiplicative Scale
	RERI (95% CI)	AP (95% CI)	SI (95% CI)	OR (95% CI)
Crude	2.15 (1.46–3.15)	0.45 (0.29–0.58)	2.15 (1.46–3.15)	1.29 (0.79–2.12)
Model 1	2.39 (1.59–3.61)	0.50 (0.34–0.63)	2.39 (1.59–3.61)	1.40 (0.83–2.36)
Model 2	2.09 (1.00–3.87)	0.44 (0.23–0.61)	2.29 (1.30–4.04)	1.44 (0.85–2.45)

Notes: Crude: unadjusted for any covariate; Model 1: adjusted for age, sex; Model 2: adjusted for age, sex, BMI, education level, TG abnormal, HDL-C abnormal, HbA1c abnormal, alcohol drinking, and cigarette smoking.

Abbreviations: OR, odds ratio; CI, confidence interval; RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction; SI, synergy index.

Our study showed that both SBP and DBP increased with rising WC, which elevated the prevalence of hypertension. This finding aligns with previous research linking WC to BP.[18–20] Central obesity, characterized by visceral fat accumulation, is associated with IR and may contribute to atherosclerosis and hypertension.[21,22] Additionally, abdominal fat can affect BP through mechanisms independent of IR, including activation of the SNS and secretion of substances that stimulate angiotensin II and aldosterone production, leading to vasoconstriction and sodium retention. Notably, adipose tissue contains a local RAAS, distinct from the systemic RAAS, which further contributes to hypertension.[23–25]

A FHH functions as both a risk factor and a predictor for the development of hypertension.[26] This condition is influenced by multiple genes, including ATP2B1, CYP17A1, and PLEKHA7, with heritability primarily driven by complex genetic contributions and environmental exposures such as high salt intake and physical inactivity.[27] Evidence from twin and family studies indicates that the heritability of hypertension ranges from 30% to 60%.[28,29] Several mechanisms have been proposed to explain the association between FHH and hypertension, including enhanced renal sodium reabsorption, decreased urinary kallikrein excretion, increased sodium-lithium countertransport activity, unfavorable high-density to low-density lipoprotein ratios, elevated serum uric acid levels, and increased oxidative stress.[26,30,31]

Although both CO and FHH are established risk factors for hypertension, studies examining their interaction, particularly in patients with T2DM are limited. Our previous work demonstrated a significant additive interaction between BMI and a family history of dyslipidemia on the risk of dyslipidemia among T2DM patients.[32] While that study focused on lipid metabolism and generalized obesity, the present study advances the field by focusing on central obesity (measured by WC rather than BMI), and by targeting hypertension as the outcome of interest. This distinction is important, as CO more accurately reflects visceral fat accumulation, which plays a direct role in hypertension pathogenesis. Furthermore, hypertension and dyslipidemia, although related, have distinct physiological pathways. To our knowledge, this is the first study in a Chinese T2DM population to demonstrate this interaction with both additive and multiplicative modeling frameworks. These findings add new evidence to the literature by highlighting a compounded risk mechanism involving central adiposity and familial predisposition, thus providing a more refined approach to hypertension risk stratification in T2DM.

Interactions can be evaluated on two scales: multiplicative and additive. A multiplicative interaction assesses whether the joint effect of two factors differs from the product of their individual effects, whereas an additive interaction evaluates whether their combined effect exceeds the sum of their individual effects. While neither scale is universally preferred, the additive scale may be more clinically meaningful, as it quantifies the proportion of risk attributable to their combined influence. We report results on both the additive and multiplicative scales to facilitate comparison with other studies. Additive interaction analysis revealed a synergistic effect of CO and FHH on hypertension in patients with T2DM, demonstrating that their coexistence significantly increases the risk of hypertension beyond their individual contributions. This synergistic effect likely arises from interconnected genetic, metabolic, and environmental mechanisms. Central obesity promotes IR, chronic inflammation, overactivation of RAAS, and increased SNS activity, all of which raise BP. Simultaneously, FHH reflects both genetic predisposition and shared lifestyle factors that enhance these processes,

creating a compounded hypertension risk. Genetic factors, including pleiotropic genes, and environmental influences such as poor dietary habits and physical inactivity, further intensify this risk in patients with both CO and FHH. Prior studies have linked obesity to hypertension,[33] pointing to pleiotropic genes that simultaneously influence multiple traits.[34] For instance, research on an Omani family revealed positive correlations across various obesity indicators (BMI, WC, WHtR) and both ambulatory and office BP measurements.[35] Genetic correlations between obesity and hypertension traits were stronger than environmental correlations.[35] However, the familial link between adiposity and BP remains debated. The Quebec Family Study found a moderate association influenced by both genetic and environmental factors,[36] whereas the HERITAGE Family Study found no evidence of pleiotropy between resting BP and body composition.[37]

Our findings provide new insights into the genetic and environmental factors contributing to hypertension risk in patients with T2DM and offer guidance for prevention and management. Clinicians should prioritize regular BP monitoring for patients with T2DM who have CO, especially those with a FHH. For such individuals, maintaining a healthy WC should be a primary preventive strategy, as WC is a direct indicator of central adiposity and a more reliable predictor of hypertension than BMI alone. Interventions should not only address glycemic control but also target CO management through lifestyle changes, including weight loss, dietary improvements, and physical activity aimed at reducing abdominal fat. Furthermore, genetic counseling and FHH assessments may help guide more personalized risk-reduction strategies. Early lifestyle interventions targeting abdominal fat in individuals with FHH may help prevent or delay hypertension onset in adulthood.

Limitations of the Study

Our study also has several limitations that should be acknowledged. First, the cross-sectional nature of our study design precludes causal inference. Second, the reliance on self-reported behavioral data may introduce recall bias. Third, while our study provides valuable insights into the regional context, validation in more diverse populations is needed to generalize our findings. Finally, despite controlling for key confounders, residual confounding factors may still have influenced the results. Future research should employ longitudinal designs to elucidate temporal relationships and explore specific gene-environment interactions.

Conclusion

Central obesity and a FHH exhibit a significant synergistic effect, increasing the risk of hypertension in patients with T2DM. These findings highlight the clinical importance of routine WC monitoring, particularly in T2DM patients with FHH, as a simple and cost-effective tool for hypertension risk stratification in resource-limited settings. Beyond hypertension prevention, our results suggest that CO may amplify genetic predispositions to other cardiometabolic disorders, potentially through pathways such as chronic low-grade inflammation or IR. Future studies should focus on longitudinal assessments of WC trajectories in relation to hypertension onset, genomic analyses to identify modifier genes influencing the WC–FHH interaction, and clinical trials evaluating the efficacy of lifestyle interventions in this high-risk subgroup.

Ethics Statement

This study was conducted in compliance with the Declaration of Helsinki. The original national study was approved by the Ethics Committee of Shanghai Jiao Tong University Affiliated Sixth People's Hospital (Approval No: 2018-010), and written informed consent was obtained from all participants. Zhejiang Province was one of the participating sites in the national study. As this study involved a secondary analysis of de-identified data, the Institutional Review Board of the Zhejiang Provincial Center for Disease Control and Prevention granted an ethics waiver in accordance with institutional policy.

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Disclosure

The authors declared no conflicts of interest in this work.

References

1. Li Y, Teng D, Shi X. et al. Prevalence of diabetes recorded in mainland China using 2018 diagnostic criteria from the American Diabetes Association: national cross sectional study. *BMJ*. 2020;369:m997. doi:10.1136/bmj.m997
2. Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas. *Diabet Res Clin Pract*. 2019;157:107843. doi:10.1016/j.diabres.2019.107843
3. Zhang YQ, Li Y, Dong YG, et al. A nationwide assessment of blood pressure control and the associated factors in Chinese type 2 diabetes mellitus patients. *J Clin Hypertens*. 2019;21(11):1654–1663. doi:10.1111/jch.13675
4. Tatsumi Y, Ohkubo T. Hypertension with diabetes mellitus: significance from an epidemiological perspective for Japanese. *Hypertens Res*. 2017;40 (9):795–806. doi:10.1038/hr.2017.67
5. Tang N, Ma J, Tao R, et al. The effects of the interaction between BMI and dyslipidemia on hypertension in adults. *Sci Rep*. 2022;12(1):927. doi:10.1038/s41598-022-04968-8
6. Ren H, Guo Y, Wang D, Kang X, Yuan G. Association of normal-weight central obesity with hypertension: a cross-sectional study from the China health and nutrition survey. *BMC Cardiovasc Disord*. 2023;23(1):120. doi:10.1186/s12872-023-03126-w
7. Hou XH, Wang LM, Chen SY, et al. Data Resource Profile: a Protocol of China National Diabetic Chronic Complications Study. *Biomed Environ Sci*. 2022;35(7):633–640. doi:10.3967/bes2022.078
8. Kendler KS, Gardner CO. Interpretation of interactions: guide for the perplexed. *Br J Psychiatry*. 2010;197(3):170–171. doi:10.1192/bjp.bp.110.081331
9. Knol MJ, van der Tweel I, Grobbee DE, Numans ME, Geerlings MI. Estimating interaction on an additive scale between continuous determinants in a logistic regression model. *Int J Epidemiol*. 2007;36(5):1111–1118. doi:10.1093/ije/dym157
10. Hosmer DW, Lemeshow S. Confidence interval estimation of interaction. *Epidemiology*. 1992;3(5):452–456. doi:10.1097/00001648-199209000-00012
11. Correia K, Williams PL. Estimating the Relative Excess Risk Due to Interaction in Clustered-Data Settings. *Am J Epidemiol*. 2018;187 (11):2470–2480. doi:10.1093/aje/kwy154
12. Owolabi EO, Ter Goon D, Adeniyi OV. Central obesity and normal-weight central obesity among adults attending healthcare facilities in Buffalo City Metropolitan Municipality, South Africa: a cross-sectional study. *J Health Popul Nutr*. 2017;36(1):54. doi:10.1186/s41043-017-0133-x
13. Zhang G, Yu C, Zhou M, Wang L, Zhang Y, Luo L. Burden of Ischaemic heart disease and attributable risk factors in China from 1990 to 2015: findings from the global burden of disease 2015 study. *BMC Cardiovasc Disord*. 2018;18(1):18. doi:10.1186/s12872-018-0761-0
14. Zhang M, Shi Y, Zhou B, et al. Prevalence, awareness, treatment, and control of hypertension in China, 2004–18: findings from six rounds of a national survey. *BMJ*. 2023;380:e71952.
15. Franklin SS, Thijs L, Li Y, et al. Masked hypertension in diabetes mellitus: treatment implications for clinical practice. *Hypertension*. 2013;61 (5):964–971. doi:10.1161/HYPERTENSIONAHA.111.00289
16. Pechere-Bertschi A, Greminger P, Hess L, Philippe J, Ferrari P. Swiss Hypertension and Risk Factor Program (SHARP): cardiovascular risk factors management in patients with type 2 diabetes in Switzerland. *Blood Press*. 2005;14(6):337–344. doi:10.1080/08037050500340018
17. Jia G, Sowers JR. Hypertension in Diabetes: an Update of Basic Mechanisms and Clinical Disease. *Hypertension*. 2021;78(5):1197–1205. doi:10.1161/HYPERTENSIONAHA.121.17981
18. Sun JY, Hua Y, Zou HY, et al. Association Between Waist Circumference and the Prevalence of (Pre) Hypertension Among 27,894 US Adults. *Front Cardiovasc Med*. 2021;8:717257. doi:10.3389/fcvm.2021.717257
19. Sun JY, Ma YX, Liu HL, et al. High waist circumference is a risk factor of new-onset hypertension: evidence from the China Health and Retirement Longitudinal Study. *J Clin Hypertens*. 2022;24(3):320–328. doi:10.1111/jch.14446
20. Zhao Y, Zhang M, Luo X, et al. Association of 6-year waist circumference gain and incident hypertension. *Heart*. 2017;103(17):1347–1352. doi:10.1136/heartjnl-2016-310760
21. Jayawardena R, Sooriyaarachchi P, Misra A. Abdominal obesity and metabolic syndrome in South Asians: prevention and management. *Expert Rev Endocrinol Metab*. 2021;16(6):339–349. doi:10.1080/17446651.2021.1982381
22. Gupta RD, Parray AA, Kothadia RJ, et al. The association between body mass index and abdominal obesity with hypertension among South Asian population: findings from nationally representative surveys. *Clin Hypertens*. 2024;30(1):3. doi:10.1186/s40885-023-00257-2
23. Zhou M-S, Schulman IH, Zeng Q. Link between the renin–angiotensin system and insulin resistance: implications for cardiovascular disease. *Vasc Med*. 2012;17(5):330–341. doi:10.1177/1358863X12450094
24. Giacchetti G, Faloia E, Mariniello B, et al. Overexpression of the renin-angiotensin system in human visceral adipose tissue in normal and overweight subjects. *Am J Hypertens*. 2002;15(5):381–388. doi:10.1016/S0895-7061(02)02257-4
25. Poirier P, Lemieux I, Mauriege P, et al. Impact of waist circumference on the relationship between blood pressure and insulin: the Quebec Health Survey. *Hypertension*. 2005;45(3):363–367. doi:10.1161/01.HYP.0000155463.90018.dc
26. Kc K, Katwal S, Yadav GK, et al. Family history of hypertension and its relation to other variables in hypertensive patients: a cross-sectional study from a tertiary care hospital. *IJS Global Health*. 2023;6(5). doi:10.1097/GH9.0000000000000235.
27. Seidel E, Scholl UI. Genetic mechanisms of human hypertension and their implications for blood pressure physiology. *Physiol Genomics*. 2017;49 (11):630–652. doi:10.1152/physiolgenomics.00032.2017

28. Shih PA, O'Connor DT. Hereditary determinants of human hypertension: strategies in the setting of genetic complexity. *Hypertension*. 2008;51 (6):1456–1464. doi:10.1161/HYPERTENSIONAHA.107.090480
29. Snieder H, Hayward CS, Perks U, Kelly RP, Kelly PJ, Spector TD. Heritability of central systolic pressure augmentation: a twin study. *Hypertension*. 2000;35(2):574–579. doi:10.1161/01.HYP.35.2.574
30. Munzel T, Gori T, Bruno RM, Taddei S. Is oxidative stress a therapeutic target in cardiovascular disease? *Eur Heart J*. 2010;31(22):2741–2748. doi:10.1093/eurheartj/ehq396
31. Ranasinghe P, Cooray DN, Jayawardena R, Katulanda P. The influence of family history of hypertension on disease prevalence and associated metabolic risk factors among Sri Lankan adults. *BMC Public Health*. 2015;15(1):576. doi:10.1186/s12889-015-1927-7
32. Chen XY, Fang L, Zhang J, Zhong JM, Lin JJ, Lu F. The association of body mass index and its interaction with family history of dyslipidemia towards dyslipidemia in patients with type 2 diabetes: a cross-sectional study in Zhejiang Province, China. *Front Public Health*. 2023;11:1188212. doi:10.3389/fpubh.2023.1188212
33. El MP, Wahoud M, Allam S, Chedid R, Karam W, Karam S. Hypertension Related to Obesity: pathogenesis, Characteristics and Factors for Control. *Int J Mol Sci*. 2022;23(20):1.
34. Shams E, Kamalumpundi V, Peterson J, Gismondi RA, Oigman W, de Gusmao CM. Highlights of mechanisms and treatment of obesity-related hypertension. *J Hum Hypertens*. 2022;36(9):785–793. doi:10.1038/s41371-021-00644-y
35. Man T, Nolte IM, Jaju D, et al. Heritability and genetic correlations of obesity indices with ambulatory and office beat-to-beat blood pressure in the Oman Family Study. *J Hypertens*. 2020;38(8):1474–1480. doi:10.1097/HJH.0000000000002430
36. Rice T, Province M, Perusse L, Bouchard C, Rao DC. Cross-trait familial resemblance for body fat and blood pressure: familial correlations in the Quebec Family Study. *Am J Hum Genet*. 1994;55(5):1019–1029.
37. An P, Rice T, Gagnon J, et al. Cross-trait familial resemblance for resting blood pressure and body composition and fat distribution: the HERITAGE family study. *Am J Hum Biol*. 2000;12(1):32–41. doi:10.1002/(SICI)1520-6300(200001/02)12:1<32::AID-AJHB5>3.0.CO;2-6